REMARKS

Claims 1-20 are pending in the application. Claims 2, 3, 5-7, 10, and 11 have been cancelled by this amendment. New claims 22-24 have been added to the application. Therefore, claims 1, 4, 8, 9, 12-20, and 22-24 are at issue.

Claim 1 has been amended to incorporate the features of originally filed and now-cancelled claims 2, 5, 6, and 7, which serve as support for this amendment. New claim 22 recites the features of originally filed claims 1, 3, 5, 10, and 11, which serve as support for this new claim. Support for new claims 23 and 24 can be found in the specification at page 4, lines 17-20 and page 9, lines 18-20. Claim 20 has been amended to correct the form of the claim. Several dependent claims have been amended to correct the dependencies of the claims.

The application now contains two independent claims, i.e., claims 1 and 22. Independent claim 1 recites a soft shell capsule having a gelatin-containing shell that encapsulates a solution formulation containing about 1% to about 45% by weight of Compound A and a pharmaceutically acceptable carrier comprising a solvent selected from propylene glycol, polyethylene glycol 400, glycofurol, and mixtures thereof. Dependent claim 8 recites polyvinylpyrrolidone as an additional component of the carrier. Claim 9 recites a preferred pharmaceutical formulation of claim 1.

Independent claim 22 recites a soft shell capsule having a gelatin-containing shell that encapsulates a suspension formulation containing about 1% to about 45% by weight of Compound A and a pharmaceutical-

ly acceptable carrier containing (a) a suspending agent and (b) a solvent selected from the group consisting of polyethylene glycol 400, propylene glycol, glycofurol, a C_8-C_{10} monoglyceride, and mixtures thereof. Dependent claim 14 recites a surfactant as an additional component of the carrier. Claims 12, 13, and 15 recite preferred embodiments of claim 22. Claim 4 recites that Compound A is present in the suspension formulation as a free drug.

Multiple dependent claims 16-19 recite additional preferred embodiments of claims 1 and 22. Claim 20 recites a method treating sexual dysfunction using a soft capsule of claim 1 or 22. Claims 23 and 24 recite specific sexual dysfunctions treated by the claimed soft capsules.

As set forth in the specification, Compound A has an extremely low water solubility. The solvents capable of dissolving Compound A, e.g., dimethyl sulfoxide, are not pharmaceutically acceptable. The present invention is directed to capsules containing a solution or suspension of Compound A such that the compound does not degrade chemically over time, and is present in a sufficient amount such that the capsule is sufficiently small for practical oral administration. After substantial research, it was found that the claimed formulations meet all of the parameters necessary to provide a useful capsule for the oral administration of Compound A.

Claim 20 stands objected to as being in improper form. Applicants have amended claim 20 to properly refer to the claims recited in the multiple dependent claim in the alternative. It is submitted that

the amendment to claim 20 overcomes the objection under 37 C.F.R. §1.75(c), and that the objection should be withdrawn.

Claims 9 and 15 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite because of a lack of antecedent for a phrase recited in each claim. Applicants have amended claims 1 and 9, and added new claim 22, which provide an antecedent basis for all features recited in claims 9 and 15, respectively. Accordingly, it is submitted that the rejection of claims 9 and 15 under 35 U.S.C. §112, second paragraph, has been overcome and should be withdrawn.

Claims 1-6, 8, 10, and 16-20 stand rejected under 35 U.S.C. §102(b) as being anticipated by WO 97/03675 (WO '675). Claims 1-6, 8, 10, 14, and 16-20 stand rejected under 35 U.S.C. §103 as being unpatentable over WO '675. Claims 1, 7, 10, and 11 stand rejected under 35 U.S.C. §103 as being unpatentable over WO '675 in view of WO 99/30697 (WO '697). In view of the amendments to the claims, and for the reasons set forth below, it is submitted that these rejections are in error and should be withdrawn.

WO '675 teaches the use of Compound A in the treatment of sexual dysfunction. WO '675 further teaches that Compound A can be orally administered as a capsule containing 0.2-400 mg of Compound A in a pharmaceutically acceptable carrier. The composition containing Compound A can include excipients or suspending agents. Pages 15 and 16 of WO '675 provide capsule formulations of Compound A. The formulations contain an active agent, lactose, polyvinylpyrollidone, mag-

nesium stearate, microcrystalline cellulose, sodium lauryl sulfate, crospovidone, and/or LABRAFIL® M 1944 CS.

LABRAFIL® M 1944 CS is an alcoholysis/esterification reaction product of apricot kernel oil and PEG300, and is described chemically as oleoyl macrogol-6 glycerides. LABRAFIL® M 1944 CS is a well-defined mixture of mono-, di-, and triglycerides and mono- and di-fatty esters of PEG. The predominant fatty acid is oleic acid (C18:1).

Capsule examples 1 and 2 at pages 15 and 16 of WO '675 contain *solid* particles and are not a solution or a suspension capsule formulation. In particular, the active ingredient, lactose, and magnesium stearate of example 1 are *all* solids and account for over 99% of the formulation. The polyvinylpyrrolidone (PVP) also may be a solid because exact form of the PVP, i.e., solid or solution, is not disclosed. Thus, capsule example 1 may be a 100% solid formulation.

Similarly, example 2 is a solid because the active ingredient, microcrystalline cellulose, and magnesium stearate are *all* solids and account for 98.5% of the formulation. The sodium lauryl sulfate and crospovidone also may be solids. Thus, example 2 also may be a 100% solids formulation.

Capsule examples 1 and 2, therefore, are merely mixtures of solids and are substantially different from the claimed solution and suspension capsule formulations. These examples absolutely fail to teach or suggest a solution or suspension capsule formulation that is stable over time.

Capsule example 3 at page 16 of WO '675 is a suspension that contains only active ingredient and LABRAFIL® M 1944 CS. This example does not teach or suggest a solution formulation of claim 1, and is substantially different from the suspension formulation of claim 22, which recites a suspending agent and solvent substantially different from LABRAFIL® M 1944 CS. LABRAFIL® M 1944 CS, as discussed above, is oleoyl macrogol-6 glycerides, which is substantially different in chemical identity from the solvents and suspending agent recited in claim 22.

In summary, WO '675 absolutely fails to teach or suggest a capsule containing a solution formulation as recited in claim 1 and claims depending therefrom. WO '675 does not even consider or address using a solvent recited in claim 1 and provides no incentive for a person skilled in the art to utilize a claimed solvent with any reasonable expectation of providing a stable and effective *solution* capsule formulation containing the highly insoluble Compound A. WO '675 also fails to teach or suggest the preferred embodiments of a solution capsule formulation recited in claim 9.

WO '675 also fails to teach or suggest a suspension capsule formulation as recited in claim 22 and claims depending therefrom. The sole suspension formulation recited in WO '675 fails to recite a formulation containing *either* a solvent as presently recited in claim 22 *or* a suspending agent. WO '675 provides no motivation or incentive for a person skilled in the art to substitute a claimed solvent and suspending agent for LABRAFIL® M 1944 CS with any reasonable expectation of providing a stable and effective *suspension* formula-

tion containing Compound A. In particular, LABRAFIL® M 1944 CS is a substantially different chemical identity from the claimed solvents and suspending agent. WO '675 also fails to teach or suggest the preferred embodiment of a suspension capsule formulation recited in claim 15. Claim 15 recites specific solvents and suspending agents that are neither addressed nor considered in the WO '675 reference.

WO '675 further fails to teach or suggest the preferred embodiments recited in claims 12 and 13, as recognized by the examiner, because these claims were not rejected over the cited references but merely objected to. WO '675 further fails to teach or suggest a suspension formulation containing a surfactant, but merely includes a surfactant in a solid formulation (capsule example 2 at page 15).

All claimed solution and suspension capsule formulations are novel and nonobvious, as opposed to a mere optimization of the capsules disclosed in WO '675. The novelty and nonobviousness of the claimed invention does not lie in Compound A or its ability to treat sexual dysfunction. The *claimed* invention is directed to capsules containing a stable solution or suspension formulation of Compound A. It is the capsule and formulations encapsulated therein that are claimed, and the claimed formulations are neither taught nor suggested by WO '675 for the reasons set forth above.

Because of a difference exists between the claimed invention and the teachings of WO '675, WO '675 cannot anticipate *any* pending claim. For the reasons set forth above, a person skilled in the art would not have had any motivation or incentive to modify the

teachings of WO '675 with any reasonable expectation of providing a presently claimed, stable solution or suspension capsule formulation. Accordingly, no pending claim would have been obvious over WO '675.

WO '697 does not overcome the deficiencies of WO '675 and thereby, in combination with WO '675, render the present claims obvious. WO '697 is directed to a combination treatment using a PDE5 inhibitor and an α-adrenergic receptor antagonist to treat impotence. WO '697 contains an extensive list of PDE5 inhibitors known at the time of filing the cited reference. This extensive list includes Compound A.

WO '697 also discloses that the combination treatment can be administered using various dosage forms, e.g., "solutions, suspensions, tablets, pills, capsules, powders, and the like" (page 17, lines 17-18). WO '697, like WO '675, teaches using *solid* compositions (e.g., lactose and milk sugar), as well as high molecular weight polyethylene glycols (see WO '697, page 17, lines 24-25), in gelatin capsules. WO '697 fails to teach a suspension or a solution composition encapsulated in a gelatin capsule.

There is no motivation from the teachings of WO '697, taken together with the teachings of WO '675, for a person skilled in the art to make the extensive modifications needed to arrive at the presently claimed solution and suspension capsule formulations. WO '697 merely discloses a wide variety of PDE5 inhibitors that have vastly different physical properties, such as solubility, from one another. WO '697 also merely generally suggests capsules. However, WO '697 fails to

teach *any* solution or suspension capsule formulations, let alone a capsule formulation containing Compound A.

In arriving at the presently claimed solution and suspension capsule formulations, the particular physical properties of Compound A had to be considered to arrive at stable solution and suspension formulations. WO '697 provides absolutely *no* teaching, suggestion, or guidance for a person skilled in the art to arrive at the presently claimed capsule formulations, even when combined with WO '675.

In particular, WO '697 is limited in its teachings to (a) disclosing Compound A among a laundry list of PDE5 inhibitors, (b) that the dosage form may be a capsule, (c) that the capsule formulation is a solid, and (d) that a high molecular weight polyethylene glycol may be present in the capsule formulation. In addition, WO '697 discloses a *combination* of a PDE5 inhibitor and an α-adrenergic receptor antagonist. A capsule formulation containing this combination would be different from a capsule formulation containing only Compound A as the active ingredient because the physical properties of the α-adrenergic receptor antagonist also must be considered.

For all of the reasons set forth above, it is submitted that pending claims 1, 4, 8, 9, 12-20, and 22-24 would not have been obvious over WO '675 in combination with WO '697. In particular, the combination of references fails to teach a gelatin shell encapsulating a solution or suspension capsule formulation as presently claimed. It is irrelevant that the cited references teach compounds that treat erectile dysfunction because the claims are directed to capsules

and particular solution and suspension formulations encapsulated within the capsule. The cited references fail to teach or suggest the claimed encapsulated formulations that are stable and avoid degradation of Compound A.

Accordingly, it is submitted that the rejection of the pending claims under 35 U.S.C. §102(b) and 35 U.S.C. §103 over WO '675, alone or in combination with WO '697, should be withdrawn. An early and favorable action on the merits is respectfully requested.

Should the examiner wish to discuss the foregoing, or any matter of form in an effort to advance this application toward allowance, the examiner is urged to telephone the undersigned at the indicated number.

Respectfully submitted,

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